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PSYCHIATRIC ASPECTS OF EPILEPTIC AND BRAIN-DAMAGED CHILDREN*

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These lectures are a study of the interaction of physiological effects of epilepsy and brain damage with other modifying factors; in particular, on the one hand, the constitutional make-up of the child—that is, factors existing prior to the injury or epilepsy—and on the other the environmental handling of the child subsequent to the injury or epilepsy.

Current Concepts of Epilepsy

Before considering the psychological effects of epilepsy and brain damage it is necessary to make a few general remarks on current concepts of epilepsy itself. In the past 20 years the study of epilepsy has been one of the most rapidly expanding fields in medicine, and it illustrates very well the two-way traffic of ideas between laboratory and clinic that is responsible for so many of the modern advances in medical knowledge. Much of the advance in both clinic and laboratory has come about from the refinement of techniques of recording electrical activity of the nervous system, whether at the microscopic level with electrodes inserted into single neurones or at the macroscopic level as seen in routine clinical electroencephalography. The new knowledge has confirmed the essential soundness of Hughlings Jackson's approach to the whole problem of epilepsy. It cannot be reiterated too often that, as he said, it is always a symptom and not a disease. As in many other symptoms in general medicine, the clinical phenomena are produced by a particular class of physiological disturbance. In the case of epilepsy we see the positive effects of an excessive, self-sustained, spontaneous discharge of neurones together with the negative effects that result from the loss of function carried out by these abnormally discharging neurones. Epilepsy would seem to be the almost unavoidable risk of the fact that the structure of the nervous system consists of excitable elements able to influence one another, and so arranged that explosions of uncontrolled overactivity can easily occur.

In the majority of cases, both clinically and experimentally, the epileptic discharge begins in a particular area, a focus of abnormal excessive excitability whose activity sooner or later involves all the rest of the brain. Occasionally, however, the whole brain seems to reach a level of abnormal excitability. This can be produced experimentally by the injection of convulsant drugs such as metrazol, and is seen clinically most often in the febrile convulsions, and probably also in certain other

convulsions associated with toxic and metabolic disorders. However, even in these cases it is uncertain whether the discharges are from a simultaneous overactivity of all neurones, or whether, even here, certain areas of the brain, perhaps in the mid-brain regions, are first of all excited to the point of spontaneous discharge, the cortex then following.

The problems of the classification of epilepsy have often been discussed by various colleagues recently; for example, Symonds (1955), Williams (1956), Masland (1960). Most books give an indefensible mixture of categories. For instance, they mix clinical fit-pattern—*petit mal*—with precipitating factors (for example, spasmophilia), causal factors such as traumatic epilepsy, and apparent clinical entities such as idiopathic epilepsy. Table I, taken from a recent review (Pond, 1958), provides the basis of the subsequent discussion. So far as possible this table is based on physiological mechanisms and pathways underlying the various seizure patterns. The forms of epilepsy which will be particularly referred to are *petit mal* of primary centrencephalic origin and the so-called temporal-lobe epilepsies. The fit-pattern of the former is too well known to need description, but surprisingly little is known about its exact physiological origin, mainly because no equivalent has ever been obtained experimentally. Most of the evidence points to the non-specific thalamic reticular system as being the probable site of the primary discharge (Gastaut and Fischer-Williams, 1959). The most important functions of this region are probably connected with attention, consciousness, or vigilance, and it is necessary to remember that there are corticofugal connexions as well as corticopetal fibres.

The so-called temporal-lobe epilepsies are perhaps better called the rhinencephalic epilepsies, since these complex seizures arise probably from the uncus, amygdaloid, and hippocampal areas and not the temporal cortex. This area has been called the visceral brain, but functions other than the autonomic control of the viscera are probably connected with this region. Other areas of the cortex (for example, the premotor region) also influence parts of the autonomic nervous system.

A minute analysis of fit-patterns, especially of minor attacks, together with a consideration of relevant E.E.G. data, is essential in order to understand the psychological problems with which these lectures will mainly deal.

Although in every case one hopes to be able to classify the patient's epileptic attacks in terms of fit-pattern and aetiology, in practice there are many cases in which

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one cannot do so. Several exhaustive investigations of epilepsies—for example, Alström (1950) and my own less intensive study of epilepsies in general practice—agree in finding that nearly 50% of adult epilepsies, but a lower proportion of childhood epilepsies, are of unknown aetiology. This latter term is much to be preferred to the term “idiopathic epilepsy,” which seems to imply a clinical entity.

Prevalence

It is extremely difficult to get an unselected sample of children with epilepsy, since the symptom may be associated with so many other different conditions. In general, children with febrile convulsions are much less often seen by a specialist of any sort than other forms of epilepsy. Children with obvious neurological defects will tend to be seen by neurologists; children who have attacks associated with general illnesses will come under the purview of paediatricians; and those seen at child-guidance clinics will, by definition, be those with conspicuous behaviour disorders as well. The biased nature of medical statistics drawn from hospital data has been generally recognized in recent years, and general practice surveys of all sorts of conditions are now very fashionable.

Pond, Bidwell, and Stein (1960) and Pond and Bidwell (1960) recently carried out a survey of epileptics in 14 general practices. The data obtained in this survey relevant to these lectures concern the prevalence of behaviour disorders in epileptic children. About a quarter of the approximately one hundred children in the survey showed significant psychological difficulties. Of the adults who had had epilepsy at school age, one-sixth had also had psychological difficulties. The survey also showed that the presence of these difficulties was of considerable prognostic significance, since the adults who had had school difficulties with epilepsy do much worse as regards occupation and social adaptation than those who had had epilepsy in childhood but without any educational or behavioural difficulties. There was a considerable excess of social class V amongst the young adult male epileptics, and the clinical histories of this group of patients showed that they were severely handicapped as regards the number and severity of the fits as well as their intellectual and personality problems. These patients may be contrasted with the children in these series who had convulsions at the so-called febrile convulsion age—that is, 1½–3 years. They had a very low incidence of associated psychological difficulties. The

existence of this group is important evidence against the view that epilepsy must necessarily imply psychological difficulties.

Intelligence of Epileptics

Almost all the patients seen in the epileptic clinic of the Maudsley Children's Department have the same full routine work-up as the other patients, including intelligence tests and full psychological and social histories. In this way data have been obtained from epileptic children in every way comparable to those on the non-epileptic child psychiatric population.

According to Nuffield (1961), the distribution of the intelligence level of the epileptic children seen at the clinic is on the average a little below normal, but this is similar to the non-epileptic child-guidance population seen at the Maudsley. The significance of the sample tested is shown by comparing this figure with that obtained by Collins (1951) testing Lennox's private out-patients. She got a mean score of nearly 104 in the normal distribution.

Following Lennox, we may classify the main factors affecting the intellectual level of epileptic children as follows: (1) a genetic influence; (2) an acquired lesion of the brain prior to the onset of the seizures; (3) the epileptic attacks themselves; (4) social and psychological factors; (5) the effects of anticonvulsant drugs.

Twin studies provide the clearest evidence for genetic factors, and reference should be made to Lennox (1960) for the details of the large amount of material that he has collected over the years. His series of monozygotic twins, one or both of them having epilepsy uncomplicated by brain injury, have average intelligence and there was no significant difference in the scores between the twins with epilepsy and those without.

The influence of brain damage on intelligence will be discussed more fully in the second lecture.

The associations between intelligence level and the form and frequency of fits themselves are complex and difficult to separate from the effects of the underlying brain damage. It is generally accepted (Metrakos and Metrakos, 1960) that children with true petit mal do not suffer any significant intellectual impairment even when the attacks are very frequent, such as is found in the condition that was formerly termed “pyknolepsy.” On the other hand, patients with frequent major seizures are usually on large quantities of anticonvulsants as well, and therefore the slowing commonly found with them may have more than one cause. Lennox found

TABLE I.—*Classification of Epilepsy*

	Group 1: Generalized Epilepsies		Group 2: Partial Epilepsies	
	Primary Subcortical (Centrencephalic)	Secondary Subcortical	Rhinencephalic (or Temporal Lobe)	Isocortex
Fit-pattern	Petit mal ± grand mal	Petit mal ± generalized myoclonic ± grand mal	“Psychomotor” ± grand mal	Focal cortical (Jacksonian) ± grand mal
Electroencephalogram:				
(a) Inter-seizure ..	Symmetrical spike-and-wave transients	Irregular spike-and-wave or focal temporal	Temporal lobe spikes (often only in sleep)	Normal or focal spikes
(b) Ictal	Three-per-second spike-and-wave	Variable but generalized and irregular spikes and spike-and-wave complexes	Complex progressive, usually symmetrical patterns of slow activity	Various, often focal only
Aetiology	Predominantly genetic. Sometimes febrile precipitation of grand mal	Various, predominantly diffuse brain damage (e.g., anoxia)	Various, mainly trauma and infections	As above
Age of onset	Petit mal from 4–10 years. Grand mal from 1½–3 years	From birth	From age 4 years	Any age
I.Q.	Normal	Often subnormal	Normal or subnormal	Normal
Personality	Normal or minor neurotic traits	No specific changes	Severe behaviour disorders	No specific changes, usually normal
Treatment	Diones ± amphetamine and phenytoin	All drugs in combination	Primidone, amphetamine, surgery	Phenobarbitone, phenytoin

that patients with what he called psychomotor attacks (that is, temporal-lobe epilepsy) had the greatest degree of intellectual backwardness, especially if the patients also had grand-mal attacks. I shall return to these points later when discussing the possible effects of epileptic activity other than in overt attacks.

We may next deal briefly with the influence of the anticonvulsant drugs. Although these have sometimes been blamed for a large part of the so-called epileptic personality (by, for example, Stauder, 1938), Lennox and various other more recent authors think they play a small part in the production of intellectual slowness. Loveland *et al.* (1957) carried out a short-term study on stable epileptics without gross psychiatric or neurological complications. On retesting of patients after only three months on drugs, no highly significant differences were found in intelligence tests and projection tests in patients compared with controls.

Chaudhry and I (1961) have recently carried out a study of epileptic deterioration; various aspects of this will be referred to later on, but in this connexion I may mention that we obtained no evidence that the length and amount of dosage of drugs contributed significantly to intellectual deterioration in epileptic children when they were compared with children who had similar evidence of brain damage and, in many cases, a similar number of epileptic attacks.

With regard to the fourth factor affecting intelligence—social and psychological environmental influences—I have no data to offer and only a few impressions. The problem with epileptic children in no way differs from the general one of how much intelligence can be increased by optimal training, and how much be decreased by neglect and especially such conditions as institutionalization. Current psychological opinion places increasing emphasis on the amount to which intelligence can be affected for better or worse by environment, and I would in general agree with this. One certainly has to take account of parental standards in assessing anomalous psychological test results, since spuriously high verbal scores can be obtained by quite dull children of intelligent and articulate parents.

The evidence so far would thus suggest that the genetic constitution is the main determinant of intelligence as in normal people, and this is affected progressively and proportionately by the amount of brain damage that also caused the fits. Social and psychological factors occupy third place, and the effects of the fits themselves and the drugs seem relatively much less important. One may compare these views with the following table from Lennox's latest work which epitomizes his changed view on the relative importance of the various factors.

TABLE II.—*Factors Affecting Intelligence of Epileptics (from Lennox, 1960)*

	Lennox		D. A. Pond
	1942	1960	
1. Heredity	20%	40%	1
2. Brain lesions a cause	15%	25%	2
3. " " lesion a result	30%	20%	4
4. Socio-psychologic factors	20%	10%	3
5. Sedative drugs	15%	5%	5

Personality Changes

The personality changes in epileptic children have been less clearly described than the psychological changes associated with epilepsy in adults. The concept of the adult epileptic personality still finds favour in

some circles, but it is now accepted that the changes seen in some adult epileptics are not the expression of hereditary degenerative stigmata but are related to acquired brain damage that has also caused the fits. In the case of children the psychiatric symptoms usually described as being typically epileptic seem to fall into two contradictory groups. On the one hand there is the explosive, irritable, overactive child; and on the other there is the slow, sticky, withdrawn, pedantic child. These symptom-groups certainly do occur in some epileptic children, but only in a minority, and the clinical pictures seen are very variable. In fact, it is safe to say that every symptom that has been found in the child psychiatric population without epilepsy has also been seen in association with epilepsy. As in the case of intelligence, there are five possible factors to consider—constitution, brain damage, the fits themselves, social and psychological factors, and the drugs.

In an earlier paper on the psychiatric aspects of epilepsy in children, published in 1952, I considered that the two main determinants of the psychological changes found were, firstly, environmental factors, and, secondly, the nature of the epilepsy from which the child suffered. My colleagues, Grunberg (1957) and Nuffield (1961), have amplified these two aspects of the subject. Working on my patients, Grunberg carried out two different but related studies. In the first he compared epileptic children with behaviour disorders, matched for sex and age with the same number of epileptic children without behaviour disorders, both groups coming from my clinic so that there was an equal amount of psychiatric and social data available. In the second comparison he compared a group of behaviour disorders with epilepsy with a group of behaviour disorders without epilepsy. He showed conclusively that epileptic children with behaviour disorders have as equally disturbed an environment as behaviour-disordered children without epilepsy, whereas stable children with epilepsy have a much lower incidence of disturbed or broken homes.

In this investigation no account was taken of the different forms of epilepsy in relation to the psychological symptoms, and in the evaluation of the latter we paid more attention to conduct disorders than to personality traits, thus perhaps overemphasizing those traits in which external environmental factors would naturally be expected to be predominant. However, the same general picture emerges from Pond and Bidwell's general-practice survey.

In contrast to this investigation, Nuffield tried to find what correlations there were between particular forms of epilepsy and behaviour disorder. He was particularly interested in the manifestations of aggressive symptoms on the one hand, as seen in temper tantrums, violence, cruelty, and so on; and in neurotic symptoms—fears, timidity, nightmares, etc.—on the other. He devised a simple rating scale for these aggressive and neurotic symptoms based on the clinical records of the patients. The E.E.G. classification is rather elaborate but corresponds broadly to Table I. Unfortunately, a number of the patients had had inadequate E.E.G. recordings for various reasons, so that an exact classification of every case was impossible. Nevertheless, it is interesting that the correlation with the behaviour ratings is a little higher in the case of E.E.G. classification than in the case of classification by fit-pattern, though both go in the same direction. Highly significant differences are found between the petit-mal child who tends to show

more neurotic symptoms and less aggression than the other groups, and the child with temporal-lobe epilepsy who shows a great deal more aggression and less neuroticism. These findings are in accord with the observations of several other authors—for example, Glaser and Dixon (1956) and Roger (1953). Somewhat surprisingly, Nuffield found that sex, age, and intelligence did not seem to be correlated with either aggression or neuroticism.

The symptoms of neuroticism and aggression were chosen by Nuffield for particular study because they are so often seen and are fairly easily rated. In addition, of course, the relationship between aggression and deep temporal-lobe lesions has also been seen in animal experiments (see Second Lecture). The relation between neuroticism and petit mal has no such clear physiological basis, though the connexion has been observed by others (for example, Bridge, 1949; Siegmund and Pache, 1953). Dr. Generali and I, in a small unpublished investigation, suspected that the passivity of these patients may also be shown by children who have no epilepsy but only abnormal responses in the E.E.G. to photic stimulation such as are often found in petit-mal children. However, there is a critical review of these data (Tizard, in press).

Amongst the many other symptoms commonly seen in epileptic children should be mentioned hyperkinesia or overactivity. Ounsted's (1955) now classical paper gives an excellent clinical description of this symptom, which is so distressing to all concerned. His paper also shows that the symptom is much commoner in boys than in girls; it is mostly seen in the pre-school years, and half of the children had I.Q.s below 70. Generalized and focal seizures of all sorts, save petit mal, are common, and there is little doubt that most if not all of the children have much brain damage. Pre-school children are more often seen by paediatricians than by child psychiatrists, which I think partly accounts for my not having seen so many of these children at the time of the overactivity. A past history of such hyperkinesia is, however, often obtained, and the transition from overactivity to underactivity (viscosity or brady-psychia) of older epileptics is one of the puzzling aspects of the influence of age on symptoms that are so far poorly understood. (In passing, I may mention that this transition is seen in brain-damaged children without epilepsy and even in non-organic problem children, as I shall discuss in my second lecture.)

The bald statistical relationship between fit-pattern and personality changes must, of course, be filled in by further data in order to understand the reason for the relationship. The question arises, for example, whether part of the variation between the different types of epilepsy may be correlated with the different social-class distribution of the various forms, or with the prevalence of broken homes. It is certainly a strong impression from the clinic that the children with petit mal tend to come from respectable middle-class homes, whereas the temporal-lobe child, who often forms the melodrama of the clinic, appears to have an unusually high proportion of broken homes. Some of the variance, therefore, may be due to some constitutional factors, a matter which I will be discussing later on. However, for what it is worth, the social-class distribution of the families of the temporal-lobe epileptics in the general practice survey did not differ from expectation. The cases of pure petit mal were too few to be analysed, and the number of temporal-lobe epileptics with psychological

problems was also too small to be compared with those without problems. The child's own reaction to having attacks is sometimes thought to be important in determining the psychiatric symptomatology. This is certainly true of neurotic reactions, which are common in adolescents but less so in younger children. However, it is interesting that the petit-mal child is so quiet and so relatively little disturbed by ordinary child psychiatric standards, in view of the great frequency of the attacks, which are also potentially dangerous because of the absence of any aura. The form of the child's response to the stress of having attacks is determined by his whole make-up and his environment.

One cannot, however, consider only the effect of epileptic attacks on the psychological state of a patient; there is also the very important way in which the psychological state of the patient influences the appearance of epileptic phenomena. Emotions play a large part in the precipitation of petit-mal attacks in children, which can be seen in interview as well as in the history of the patient. There is also the extremely small group of patients who discover for themselves the pleasure, or relief of tension, of brief but atypical petit-mal attacks that can be produced in themselves usually by flickering with their fingers while staring at the sunshine or a bright light (Sherwood *et al.*, in press). Every chronic mental hospital nurse knows the way in which chronic epileptic patients seem to be working up to a fit, with increased disturbances of behaviour, rage, violence, etc., that may culminate in status or frequent attacks, leaving the patient in a state of relative quietness for some days or weeks afterwards. It is facts like these that make one cautious in being sure whether the behaviour is due to "subclinical epilepsy" or whether the fits may sometimes appear as a result of the increasing tension and irritability manifested by the patient for other reasons.

Drugs Effects and Treatment

So far as drugs are concerned, I have already mentioned that neither Loveland *et al.* nor Chaudhry and I found convincing evidence that drugs contributed significantly to the clinical picture of intellectual deterioration, and the same holds for personality changes as well. Research into long-term drug effects is almost impossible, since the forms of epilepsy not apparently associated with serious personality change—febrile convulsions and petit mal—are never treated for long periods of years with the high doses of those drugs like primidone and phenobarbitone that are used for the temporal-lobe epileptics. One can never separate out the type of epilepsy from the drugs used.

Others besides myself have remarked on the paradoxical effects of sedative and stimulant drugs on children generally. Phenobarbitone often makes epileptic children very irritable, and primidone is a more suitable anticonvulsant in many cases. The general principles of anticonvulsant medications are well known, and I have already discussed the special problems of children (see Pond, 1958). Drugs other than anticonvulsants that are sometimes useful with the behaviour disorders are amphetamine and the tranquillizers, such as chlorpromazine, which should, of course, always be given with anticonvulsants, since they may otherwise increase the number of fits. The use of all these drugs is essentially empirical, and dosages are increased until toxicity or improvement occurs.

Much more important than the use of drugs in most cases of behaviour disorder is manipulation of the

environment of the epileptic child (Pond and Bidwell, 1954). In the last few years there has been a striking improvement in the attitude of schools to epileptic children, and it is now quite rare to have difficulty in finding a school commensurate with the child's intellectual level. Behaviour disorders cause most difficulties, and placement may be possible only after a period of in-patient stabilization such as is provided by a child psychiatric unit for the worst cases or in the epileptic colonies for the milder ones. The colonies have thus interestingly changed in function from being institutions into which children are "put away" for an indefinite period of years to being long-stay hospitals with educational facilities.

Unfortunately, this liberal attitude of schools has rather sharpened the contrast with the harsher world of employment, fitting into which makes many difficulties for handicapped children. This was very clearly brought out in my general-practice survey, as already mentioned. The implications for the proper planning for the care of epileptics in the light of these changing circumstances are elaborated in the Cohen Committee report on epileptics (1956) and in the W.H.O. monograph (1957).

There may, of course, be other clinical syndromes associated with epilepsy and of particular psychiatric interest besides petit-mal and temporal-lobe attacks, but they are not yet well delineated. However, owing to much current interest I must mention briefly the so-called infantile spasms or hypsarrhythmia (see Jeavons and Bower, 1961). This condition is well known to paediatricians, and it begins usually in the first year of life with numerous major and minor seizures of all sorts, and an arrest, even a regression, of mental development. The psychiatric interest stems from the fact that the children often become hyperkinetic, and when the fits stop after a few years, as they usually do, the child is left with mental deficiency of some degree. It is now certain that this is not an aetiological entity, and I think, in fact, that much of the epileptic phenomena, as well as the psychiatric picture, must be related to the age of the subjects and the degree, rather than site and nature, of the brain damage.

It is most important not to imagine that petit-mal attacks cause passivity or temporal-lobe fits produce aggression. One must distinguish so far as possible between behaviour disorders seen before fits, during fits, after fits, and without relation to fits (Pond, 1957). The disorders discussed here belong to this last group. The temper tantrums of the temporal-lobe child are like any other child's tantrums in appearance, though they may be more frequent and triggered off by more trivial circumstances. Likewise the neurotic tendencies of the petit-mal child do not differ from similar symptoms in non-epileptic children. The association between fit-pattern—or rather physiological disturbance as seen on both fit-patterns and E.E.G. patterns—and the behaviour is an indirect one, and there would appear to be two possible explanations: firstly, the idea of subclinical epilepsy—that is, the presence of abnormal excessive discharges in the brain not recordable by our ordinary techniques and not resulting in the usual clinical phenomena of fits; and the second possible explanation, which concerns the non-ictal effects of the associated brain damage.

In my chapter in Holzel and Tizard's book I reviewed the evidence against the idea of subclinical epilepsy. Since then I have reluctantly come to the conclusion

that there is other evidence that epileptogenic lesions may have effects over and above those seen in undoubted overt clinical epileptic attacks and not explicable simply as the direct effect of the associated brain damage. For example, after temporal lobectomy there is a clear correlation between diminution in the number of attacks and decrease in aggressive behaviour, but no correlation between chronic neurotic symptoms and control of fits (James, 1960). There is also some evidence of difference in symptomatology between epileptogenic and non-epileptogenic lesions—for example, Bingley's (1958) review of temporal-lobe tumours and temporal-lobe epilepsy. His findings are being confirmed by an investigation of mine with Serafinidis in progress which also shows up other important factors—namely, the length of history and the age of the patients.

Chaudhry and I (1961) have investigated the factors that appear to be associated with intellectual and emotional deterioration in a small proportion of epileptic children. They showed that, in contrast to the picture in adults, deterioration in children was correlated with the continuance of seizures and the failure of influence of anticonvulsants. Furthermore, the E.E.G.s of the children who had deteriorated showed both diffuse and focal changes, in contrast to a controlled group suffering from comparable types of epilepsy but no deterioration. In several cases we found patients who deteriorated for some time and then slowly began to get better when the attack came under control, either spontaneously or after a temporal lobectomy.

This work would at first sight appear to conflict with that which I quoted earlier from Lennox, who showed that in identical twins with a discordant epilepsy there is no difference between the pairs as regards intellectual level. The crucial differences are, firstly, that the form of epilepsy with which Lennox is concerned is quite different from mine, and, secondly, that his patients had not any evidence of acquired brain damage, and all mine had. The fit-patterns of the two groups are fundamentally different, his being mainly of the so-called centrencephalic variety and mine being entirely of complex temporal-lobe and generalized types.

In addition to all this clinical evidence, one should also mention the paper of Morrell *et al.* (1956) on the effects of temporal-lobe epileptogenic lesions and lobectomy on processes of conditioning and the acquisition of patterns of behaviour. They showed that lobectomy, with removal of an epileptogenic area, results in an improvement in learning capacity that had been previously diminished by the epileptogenic lesion. On the other hand, quite prolonged and widespread epileptic discharges can be recorded at operation without any apparent accompanying clinical phenomena, as is well known to electrocorticographers recording during neurosurgical procedures; for example, Pampiglione and Falconer (1960) and several other workers in other clinics. In addition, there are, of course, the frequent focal spikes which may be found in the E.E.G. of patients with focal cortical lesions, and the generalized spike-and-wave that is seen in patients with petit mal and other centrencephalic forms of attack. In neither of these groups are there usually any clinical accompaniments of these discharges, and they do not seem to interfere in any significant way with the psychological well-being of the patient.

The latest paper bearing on this is by Johnson *et al.* (1960), who report no significant change in learning and other cognitive tests given to non-epileptic subjects while

they showed generalized and widespread disruption of normal cortical activity during photic stimulation. It thus appears that only certain types of discharge, or, perhaps more accurately, discharges in certain areas rather than others, can be important in producing the psychological phenomena associated with epilepsy. The local character of the discharge invalidates the objection made on the grounds of a failure of anticonvulsants to modify such abnormal behaviour and the failure of metrazol to precipitate it. Focal epileptic activity is very difficult to control by drugs, and it is rarely produced by intravenous metrazol (though, of course, topical application may work).

Does the clinical material enable us to say anything about the psychological effects that may be associated with these forms of discharge? One can, I think, find disturbances in many areas that might be related. There

is, firstly, the crude and overt expression of sexual and aggressive functions. There are, secondly, the peculiar disturbances of consciousness, the twilight states, the apparently hysterical outbursts, the pseudo-hallucinations, and so on. There is, thirdly, the intellectual dullness and slowness which may be very marked in some patients. All these three changes may be paralleled by the effects of animal experiments, and I suspect there may be some unitary disturbance of function behind all three, the nature of which we cannot at present formulate. One can only speculate on what might be the effects of *epilepsia partialis continuans* in the amygdaloid regions by analogy with the continuous jerks produced by this type of constant discharge in the motor areas.

The second lecture, together with a list of references, will appear in our next issue.

VIRUSES ISOLATED FROM NATURAL COMMON COLDS IN THE U.S.A.*

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A new group of viruses causing common colds in human volunteers has now been cultivated in the laboratory by altering the conditions of incubation and the content of bicarbonate in the culture medium (Tyrrell *et al.*, 1960; Hobson and Schild, 1960; Tyrrell and Bynoe, 1961). Pending more complete serological definition of these agents, they are being grouped according to the type of tissue culture in which they produce a cytopathic effect. While some grow equally well in both monkey-kidney and human-kidney cultures, others grow only in human-kidney cultures.

The purpose of this report is to present the results of virus isolations from natural common colds in a group of young adults in the United States. These isolations support the aetiological role of such new viruses in natural common colds, together with some previously described viruses (E.C.H.O. 28, respiratory syncytial virus, para-influenza 1 and 2).

Materials and Methods

Study Population.—Student volunteers in the first and second preclinical years of medical training at the University of Chicago were followed throughout the eight-month academic year. The 96 men and 5 women who enrolled in this programme reported to the laboratory at the first sign of a cold and returned in two to three weeks for convalescent specimens. In addition, specimens were taken from the asymptomatic members of the group at about six-week intervals during the entire period. At each visit nasal and throat swabs were taken in duplicate. One set was placed in 0.5% bovine serum albumin in phosphate-buffered saline for inoculation into tissue cultures and the other in blood broth for bacteriological cultures performed by our clinical microbiology laboratory. A blood sample was also drawn each time. The serum was separated and stored at -20°C . The

signs and symptoms of each illness and their duration were recorded.

Tissue Culture.—Secondary monkey- and human-kidney cultures were prepared from cells which had been grown in bottles as primary cultures, and were trypsinized and frozen by the method of Stulberg *et al.* (1959). The monkey-kidney tissue was grown in 0.5% lactalbumin hydrolysate with 5% calf serum and maintained in 50% Eagle's medium and 50% medium "199." Both contained 0.2% hyperimmune rabbit antiserum to SV-5 virus. Human-kidney cultures were grown in 0.5% lactalbumin hydrolysate, 20% calf serum, and 10% medium 199 (Hsiung, 1959) and maintained in 50% Eagle's medium and 50% medium 199 with 1% calf serum. Both maintenance media also contained 0.03% sodium bicarbonate. To all media, 100 units of penicillin and 100 μg . of streptomycin per ml. were added. Both the monkey-kidney and human-kidney cultures were incubated at 33°C . on a roller drum. The H.Ep.2 cell line was carried in bottles on Eagle's medium with 10% calf serum. Tube cultures, after initial growth on the same medium, were maintained on Eagle's medium with 5% chicken serum. Incubation was at 36°C . in stationary racks. The specimens were inoculated into tissue cultures of monkey kidney, human kidney, and H.Ep.2 cells the same day on which they were obtained. The cultures were then examined for cytopathic effect three times a week and passages were made of any which appeared abnormal. Monkey-kidney cultures were tested at five-day intervals for the presence of haemadsorbing viruses by the method of Chanock *et al.* (1958).

Identification of Viruses.—Haemadsorbing viruses were identified by means of the haemadsorption-inhibition test with known antiserum (Chanock *et al.*, 1958). Respiratory syncytial virus and E.C.H.O. 28 were identified by neutralization tests with known antisera (Beem *et al.*, 1960; Hamre and Procknow, 1961).

Serological Tests.—Complement-fixation tests with respiratory syncytial virus were performed using 2 units

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